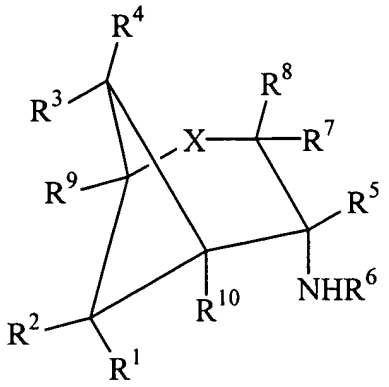
Claims

1. **(currently amended)** A compound of formula I:



(I)

wherein

R^1, R^2, R^3, R^4, R^7, R^8, R^9, and R^{10} are each independently hydrogen, carboxy, tetrazolyl, $-SO_2OH$, $-PO(OH)_2$, $-B(OH)_2$, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, cyano, halo, $-CONR_aR_b$, $-NR_cR_d$, $-SR_e$, aryl, heteroaryl, aryl$(C_1\text{-}C_6)$alkyl, diaryl$(C_1\text{-}C_6)$alkyl, or heteroaryl$(C_1\text{-}C_6)$alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy;

R^5 is carboxy, tetrazolyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $-SO_2OH$, $-B(OH)_2$, or $-PO(OH)_2$;

R^6 is hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, aryl, aryl$(C_1\text{-}C_6)$alkyl, heteroaryl, heteroaryl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxycarbonyl, or $(C_1\text{-}C_6)$alkanoyl;

X is ~~absent (a direct or single bond connects C_3 and C_4), oxy (-O-), thio (-S-), sulfinyl (-SO-), sulfonyl ($-SO_2$-), $-C(R_f)(R_g)$-, seleno (-Se-), $-P(R_x)$-, or~~ $-N(R_x)$-, wherein

R_x is hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$ -$C_6)$alkanoyl, aryl, aryl$(C_1$ -$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl, or aryl$(C_1$-$C_6)$alkoxycarbonyl;

each R_a R_b and R_e is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, aryl, heteroaryl, benzyl, or phenethyl; and

each R_c or R_d is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R_c and R_d together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;

~~R_f and R_g are each independently hydrogen, carboxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, $(C_1$-$C_6)$alkoxycarbonyl, cyano, halo, $-CONR_hR_i$, $-NN_jR_k$, $-SR_m$, aryl, heteroaryl, aryl$(C_1$-$C_6)$alkyl, or heteroaryl$(C_1$-$C_6)$alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, $(C_1$-$C_6)$alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy; or R_f and R_g together are oxo (=O) or thioxo (=S);~~

~~each R_h, R_i and R_m is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, aryl, heteroaryl, benzyl, or phenethyl; and~~

~~each R_j or R_k is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R_j and R_k together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;~~or a pharmaceutically acceptable salt or prodrug thereof;

wherein at least one of R^1, R^2, R^3, R^4, R^9, and R^{10} is carboxy, tetrazolyl, $-SO_2OH$, $-PO(OH)_2$,or $-B(OH)_2$.

2. **(original)** The compound of claim 1 wherein R^1, R^2, R^3, R^4, R^7, R^8, R^9, and R^{10} are each independently hydrogen, carboxy, tetrazolyl, $-SO_2OH$, $-PO(OH)_2$, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, cyano, halo, $-NR_cN_d$, aryl, heteroaryl, aryl$(C_1\text{-}C_6)$alkyl, diaryl$(C_1\text{-}C_6)$alkyl, or heteroaryl$(C_1\text{-}C_6)$alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy.

3. **(original)** The compound of claim 1 wherein R^1, R^2, R^3, R^4, R^7, R^8, R^9, and R^{10} are each independently hydrogen, carboxy, tetrazolyl, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkanoyl, cyano, halo, aryl, or heteroaryl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, $(C_1\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy.

4. **(original)** The compound of claim 1 wherein R^5 is carboxy, tetrazolyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $-SO_2OH$, or $-PO(OH)_2$.

5. **(original)** The compound of claim 1 wherein R^5 is carboxy.

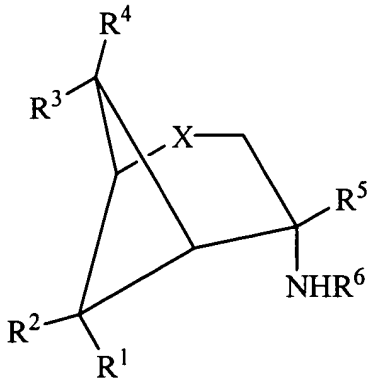
6. **(original)** The compound of claim 1 wherein R is hydrogen, $(C_1\text{-}C_6)$alkyl, aryl, aryl$(C_1\text{-}C_6)$alkyl, diaryl$(C_1\text{-}C_6)$alkyl, or $(C_1\text{-}C_6)$alkanoyl.

7. **(canceled)**

8. **(canceled)**

9. **(canceled)**

10. **(currently amended)** A compound of formula II:



(II)

wherein

R^1, R^2, R^3, and R^4, are independently hydrogen, carboxy, tetrazolyl, $-SO_2OH$, $-PO(OH)_2$, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, $(C_2\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, cyano, halo, $-CONR_aR_b$, $-NR_cR_d$, $-SR_e$, aryl, heteroaryl, aryl$(C_1\text{-}C_6)$alkyl, or heteroaryl$(C_1\text{-}C_6)$alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkyl$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C6)$alkanoyl, $(C1\text{-}C_6)$alkanoyloxy, $(C_1\text{-}C_6)$alkoxycarbonyl, cyano, nitro, trifluoromethyl, triflouromethoxy, and carboxy;

R^5 is carboxy, tetrazolyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $-SO_2OH$ or $-PO(OH)_2$;

R^6 is hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_3\text{-}C_6)$cycloalkly$(C_1\text{-}C_6)$alkyl, phenyl, benzyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkanoyl, or phenethyl;

X is ~~absent, oxy (-O-), thio (-S-), sulfinyl (-SO-), sulfonyl (-SO_2-),] -C(R_f)(R_g)-, or~~ $-N(R_X)-$, wherein R_X is hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkanoyl, phenyl, benzyl, or benzyloxycarbonyl;

each R_a, R_b, and R_e is independently hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, aryl, heteroaryl, benzyl, or phenethyl; and

each R_c or R_d is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R_c and R_d together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;

~~R_f and R_g are each independently hydrogen, carboxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkanoyl, $(C_2$-$C_6)$alkanoyloxy, $(C_1$-$C_6)$alkoxycarbonyl, cyano, halo, $-CONR_hR_i$, $-NR_jR_k$, or $-SR_m$, aryl, heteroaryl, aryl$(C_1$-$C_6)$alkyl, or heteroaryl$(C_1$-$C_6)$alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, $(C_1$-$C_6)$alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy; or R_f and R_g together are oxo (=O) or thioxo (=S);~~

~~each R_h, R_i, and R_m is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, aryl, heteroaryl, benzyl, or phenethyl; and~~

~~each R_j or R_k is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_1$-$C_6)$alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R_j and R_k together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;~~ or a pharmaceutically acceptable salt thereof;

wherein at least one of R^1, R^2, R^3, and R^4 is carboxy, tetrazolyl, or $-SO_2OH$.

11. **(canceled)**

12. **(canceled)**

13. **(original)** A pharmaceutical composition comprising a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

14. **(currently amended)** A therapeutic method for ~~preventing or~~ treating a pathological condition or symptom in a mammal which is associated with abnormal activity of a metabotropic glutamate receptor, comprising administering to a mammal in need of such therapy, an effective amount of a compound of claim 1.

15. **(original)** The method of claim 14 wherein the condition is, or the symptom is associated with epilepsy, cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, pain, spinal cord injury, head trauma, perinatal hypoxia, cardiac arrest and hypoglycemic damage, anxiety, neurodegenerative diseases, Huntington's Chorea, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, Parkinson's Disease, or Multiple Sclerosis.

16. **(original)** The method of claim 14 wherein the condition results in progressive loss of neuronal cells and/or cellular function.

17. **(original)** The method of claim 14 wherein the condition is, or the symptom is associated with stroke.

18. **(original)** The method of claim 14 wherein the condition is, or the symptom is associated with Alzheimer's disease.

19. **(currently amended)** ~~A therapeutic method to treat or manage an addiction comprising administering an effective amount of a compound of claim 1 to a mammal in need of such therapy.~~ The method of claim 14, wherein the condition or symptom is associated with morphine dependence.

20. **(currently amended)** The compound of claim 1 comprising a detectable label, wherein said detectable label is selected from the group consisting of ^{2}H, ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{13}N, ^{15}N, and ^{18}O.

21. **(new)** A therapeutic method for preventing a pathological condition or symptom in a mammal which is caused soley by abnormal activity of a metabotropic glutamate receptor, comprising administering to a mammal in need of such therapy, an effective amount of a compound of claim 1.